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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,060	07/25/2001	Sigrid Cornelis	4976US	6077

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EXAMINER
SULLIVAN, DANIEL M

ART UNIT	PAPER NUMBER
1636	17

DATE MAILED: 02/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/915,060	CORNELIS ET AL.	
	Examin r	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cov r sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-7,11-15,23-25 and 27-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-7,11-15,23-25 and 27-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Non-Final Office Action is a response to the "Amendment" filed 3 December 2002 (Paper No. 16) in reply to the Non-Final Office Action mailed 28 August 2002 (Paper No. 15). Claims 1, 4-7, 11-17 and 23-26 were considered in Paper No. 15. Claims 1, 4-7, 11, 12, 14 and 25-28 were amended and claims 16, 17 and 26 were cancelled in Paper No. 16. Claims 1, 4-7, 11-15, 23-25 and 27-36 are pending and under consideration.

Second Preliminary Amendment

Regarding Applicant's inquiry as to the status of a Preliminary Amendment filed 23 October 2001, an amendment with a certificate of mailing dated 23 October 2001 was received in the Office on 8 January 2002. The amendment has been entered in the case. Because the amendment did not arrive until after the First Action on the Merits, it was not considered therein.

Response to Amendment

Rejections pertaining to claims 16, 17 and 26 are rendered moot by the cancellation of the claims in Paper No. 16.

Rejections Based on Xiang *et al.*

Claims 1, 4-7, 11 and 12 stand rejected under 35 U.S.C. § 102(b) as anticipated by Xiang *et al.* (1994) *J. Biol. Chem.*269:15786-15794 and claims 13-15, 23 and 24 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Xiang *et al.* for reasons of record.

Applicant traverses the outstanding rejection on the grounds that the claims are directed to a specific recombinant sequence, denominated as an IRES sequence, which enables cell-cycle dependent mRNA translation in a eukaryotic cell and thus a recombinant fragment derived from a known sequence which has specific, defined function. This argument has been fully considered but is not found persuasive because the claim language used is interpreted as open and thus reads on any nucleic acid comprising the fragments identified to have the function of an IRES sequence. Because the sequence taught by Xiang *et al.* comprises the sequence identified in the instant application to function as an IRES, and that function is inherent to the sequence, the teachings of Xiang *et al.* anticipate the claimed nucleic acid. However, it is noted that, because Xiang *et al.* does not teach any function associated with the sequence corresponding to the fragments identified in the instant application as a G2/M cell cycle-dependent IRES, it would not be obvious to excise those fragments from the nucleic acid taught by Xiang *et al.* or insert those fragments into a heterologous nucleic acid. Therefore, claims directed to the sequence set forth as SEQ ID NO:1, 4-6 or 7 comprised within a heterologous nucleic acid would be patentable over Xiang *et al.*

Rejections Based on Gururajan *et al.*

Claims 25 and 27-36 stand rejected under 35 U.S.C. § 102(a) as anticipated by Gururajan *et al.* (1998) *Genome Res.* 8:929-939 for reasons of record in Paper No. 15.

As above, Applicant traverses the outstanding rejection on the grounds that the claims are directed to a specific recombinant nucleic acid fragment derived from a known sequence which has specific, defined function. However, because the claims are again directed to nucleic acids

comprising (the Office interprets the phrase "consisting essentially of" as open with regard to nucleic acid sequences) the fragments having defined function, the claims read on any nucleic acid, such as the nucleic acids taught by Gururajan *et al.*, which comprise the sequence disclosed in the instant application. As above, because Gururajan *et al.* does not teach any function associated with the sequence corresponding to the fragments identified in the instant application as a G2/M cell cycle-dependent IRES, it would not be obvious to excise those fragments from the nucleic acid taught by Gururajan *et al.* or insert those fragments into a heterologous nucleic acid.

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6, 7, 11-15, 23 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Claims 1, and claims 11-15, 23 and 24 as they depend from claim 1, are directed to a recombinant nucleic acid sequence enabling G2/M cell cycle-dependent initiation of translation which is an IRES. The claims thus encompass a genus of any and all nucleic acid molecules having the function of a G2/M cell cycle-dependent IRES regardless of the structure. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics (see MPEP 2163 (ii)). In the instant case, the disclosure provides a single example of a nucleic acid sequence having the claimed function, and fragments of that sequence that retain function, and reduction to practice of that nucleic acid. However, the Guidelines for Written Description state "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus", "In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Federal Register, Vol. 66, No. 4, Column 2, page 71436). Clearly, the single nucleic acid sequence provided does not adequately describe the full scope of all nucleic acid sequences having the function of a G2/M cell cycle-dependent IRES. It is therefore incumbent upon Applicant to disclose the relevant identifying characteristics of the genus of nucleic acid molecules encompassed by the claims. According to the Guidelines for written description, identifying characteristics include, "structure or other physical and/or chemical properties,...functional characteristics coupled with a known or disclosed correlation between

function and structure or... a combination of such identifying characteristics..." (page 1106, column 3, second full paragraph). In Example 3, beginning on page 20, the specification discusses the importance of RNA secondary structure in IRES function and points out some predicted stem-loop structures in the disclosed sequence that appear to be analogous to stem-loop structures found in other IRES sequences. Example 3 also describes several experiments that can be performed to analyze the structural determinants of IRES function, which appear to be prophetic as no data are presented from these experiments. Although these teachings point to potential structural determinants of IRES function, the specification is silent with regard to the structural determinants of the G2/M cell cycle-dependence and thus fails to describe the characteristics which are common to the genus of nucleic acids that functions as a G2/M cell cycle-dependent IRES.

Claim 6 is directed to a recombinant nucleic acid molecule comprising a nucleotide sequence at least substantially homologous to SEQ ID NO:1 and claim 7 is directed to a nucleic acid molecule comprising a sequence hybridizing under conventional conditions to at least a part of SEQ ID NO:1. In paragraph [0053], the specification defines "substantially homologous" as at least 50% identical in sequence, and paragraph [0058] cites Sambrook (*Molecular Cloning: a laboratory manual*) in reference to conventional hybridization conditions and states that stringent conditions are a preferred embodiment. Therefore, the nucleic acid of claim 6 comprises a genus of nucleic acids having at least 50% structural identity to SEQ ID NO:1, or a fragment thereof, and the nucleic acid of claim 7 encompasses any nucleic acid molecule capable of hybridizing to SEQ ID NO:1, or a fragment thereof, under even low stringency hybridization conditions, wherein the nucleic acid molecules of claims 6 and 7 retain the function of a G2/M cell cycle-

dependent IRES. However, the structural limitations set forth in the claims pertain only to the primary nucleic acid sequence. As taught in the specification (*Id.*), the functioning of an IRES is dictated by secondary and tertiary RNA structure; therefore, a simple recitation of nucleic acid sequence, without a teaching of how that sequence will affect the function of the nucleic acid is not adequately descriptive. An adequate written description of a nucleic acid requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. It is not sufficient to define DNA solely by its principal biological property, i.e. it functions as a G2/M cell cycle-dependent IRES, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Also, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, claiming all DNA's that achieve a result without defining what means will do is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)).

In view of these considerations, a skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of nucleic acid molecules having the function of a G2/M cell cycle-dependent IRES. Therefore, only the sequences explicitly set forth in the disclosure that have been demonstrated to function as a G2/M cell cycle-dependent IRES meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 25 and 27-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are directed to a Markush group "consisting essentially of" sequences set forth as SEQ ID NO:4-6 and combinations thereof. As claimed, the Markush group appears to include species that are not set forth in the claim and is thus indefinite because the identity of those species is unknown. Based on statements made in the fifth paragraph on page 7 of Paper No. 16, it appears that Applicant intends that the claimed nucleic acid should consist essentially of the species set forth in the Markush group. That is, a recombinant nucleic acid molecule consisting essentially of a nucleic acid sequence selected from the group consisting of, etc. Amending the claim accordingly would obviate this rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-9105 for regular communications and 703-746-9105 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

dms
February 19, 2003

JAMES KETTER
PRIMARY EXAMINER